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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,843	12/22/2000	Shui-on Leung	IMMU:014US1	9659

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ROSSI, KIMMS & McDOWELL LLP.
P.O. BOX 826
ASHBURN, VA 20146-0826

EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/741,843	LEUNG ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *113 and 150-156* is/are pending in the application.

4a) Of the above claim(s) *150-154* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *113,155,156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/07 has been entered.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 113,155,156 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 113 is indefinite in that it reads on a nucleic acid encoding a chimeric antibody that has human FRs. The specification, page 8, penultimate paragraph clearly indicates that a chimeric antibody has the intact murine VK/VH (aka with naturally associated murine FRs) whilst a humanized antibody has murine CDRs and human FRs. These definitions agree with the prior art (for example see Leung et al. (Hybridoma)). Thus, the claims are indefinite because the claims under consideration encompass a nucleic acid encoding a chimeric antibody wherein said antibody would not contain human FRs (as per the definition of said term in the art and specification) whilst the claims recite that said antibody has human FRs. Therefore, it is unclear as to what chimeric antibody means in the context recited in the claim.

For the purposes of prior art the term chimeric antibody in the claim will be interpreted as per the definition of said term in the specification (aka no human FRs) and wherein it appears that it is only the humanized antibody recited in the claim which contains the human FRs.

4. As per paragraph 2 of the Office Action of 7/20/07, the previous elected species was nucleic acid encoding chimeric antibody (aka antibody of SEQ Ids 2 and 4). Therefore, claims drawn to nonelected species (nucleic acids encoding humanized

antibodies and antibody fragments) are withdrawn from consideration as drawn to nonelected species. Antibodies with substituted FR regions do not read on the elected species because they contain amino acids different from those found in the elected species and said substituted FRs are found in humanized not chimeric antibodies. It is noted that the species election of 12/18/03 referred to a nucleic acid encoding a specific antibody with a specific amino acid sequence and referred to a choice of said sequence with or without exogenous FR regions (SEQ IDs 2 and 4 versus antibody of claim 111). Murine and human FRs have different amino acid sequences and are functionally distinct (for example with regards to immunogenicity upon human administration).

5. Claims 113,155,156 are under consideration as per reading on the previously elected species (chimeric antibody, aka antibody of SEQ. IDs 2 and 4 wherein the CDRs recited in claim 113 are found in said antibody).

6. The amendment filed 10/30/07 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. The abstract raises the issue of new matter in the second line (fragments thereof), wherein there is no support for said fragments in the specification as originally filed. Regarding applicants comments, the cited passages of the specification refer to the intact VH and intact VK as "fragments of the cLL2 chimeric antibody". Said passages do not refer to fragments of chimeric antibodies and refer only to the intact VH and VK of the cLL2 antibody.
The abstract raises the issue of new matter in the recitation of "A humanized LL2 monoclonal antibody further comprises CDRs of the light and heavy chain that have been recombinantly joined to a framework sequence of human light and heavy chains variable regions" because it does not state that the FRs are attached to the CDRs only as per found attached to CDRs as is normally found in antibodies.

Applicant is required to cancel the new matter in the reply to this Office Action.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. The rejection of claims 95-100,113,115,126,127 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25-27 of U.S. Patent No. 6,187,287 for the grounds elaborated in the previous Office Action is withdrawn in view of the TD filed 10/30/07 and the cancellation of claims that have been cancelled.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. The rejection of claims 95-100,115,126,127 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as per the previous Office Action is withdrawn in view of the cancellation of said claims.

11. Claims 113, 154-156 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the nucleic acid(or vectors or cells containing said nucleic acids) of claim 113. The specification discloses nucleic acids encoding a chimeric LL2 antibody wherein said nucleic acids encode all of the CDRs and FRs derived from the murine LL2 antibody. The claims encompass nucleic acids encoding chimeric antibodies wherein the heavy and or light chain variable regions contain FR regions not derived from LL2 and there is no disclosure of such nucleic acids in the specification as originally filed. For example, there is no disclosure in the specification of chimeric antibodies with FRs derived from other murine species. Regarding applicants comments, claim 113 encompasses FRs derived from other than the parent murine LL2 antibody. The claims encompass nucleic acids encoding chimeric antibodies wherein the heavy and or light chain variable regions contain FR regions not derived from LL2 and there is no disclosure of such nucleic acids in the specification as originally filed. For example, there is no disclosure in the specification of chimeric antibodies with FRs derived from other murine species.

There is no support in the specification as originally filed for the nucleic acids encoding a chimeric antibody recited in the claims wherein said antibody has human

FRs. As per the above comments about chimeric versus humanized antibodies, there is no disclosure in the specification of a chimeric antibody with human FRs (said antibody is a humanized antibody).

There is no support in the specification as originally filed for the expression vectors of claim 154. The specification discloses use of the mammalian expression vectors of page 8, lines 7-10, but does not disclose the scope of the claimed invention which encompasses use of other expression vectors. Regarding applicants comments, Figure 3 (see brief description of drawings) and Example 3 are limited to the disclosure of the aformentioned expression vector.

There is no support in the specification as originally filed for the expression cells of claim 155. The specification discloses use of mammalian expression cells containing the mammalian expression vectors of page 8, lines 7-10, but does not disclose the scope of the claimed invention which encompasses use of mammalian expression cells which do not contain said vector..

There is no written description of the claimed inventions in the specification as originally filed (the claimed inventions constitute new matter).

8. Regarding claims 113,155,156 and the application of prior art, for the same reasons that said claims constitute new matter, they are not entitled to priority to the parent applications to which priority is claimed.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 113,155,156 are rejected under 35 U.S.C. 102(b) as being anticipated by Leung et al. (US Patent 5,789,554). Applicants arguments have been considered and deemed not persuasive.

Leung et al. teach nucleic acids encoding the chimeric LL2 antibody which contains the nucleic acids encoding the variable heavy and light chains of the murine LL2 wherein said chains have the CDRs recited in the claims (see Example 4 and Figures 4a and 4b). Leung et al. teach vectors and a myeloma host cell containing said nucleic acids (see Example 4). Regarding applicants comments, whilst Leung et al. discloses embodiments that anticipate the claimed inventions, the scope of the claims under consideration also encompass additional embodiments which constitute new matter as per above.

Regarding applicants comments, the claimed nucleic acids encoding chimeric antibodies constitute new matter (aka lack written description) as per above. Whilst claim 113 is indefinite as per above, for the purposes of prior art, the chimeric antibody recited in the claims will be interpreted as per the definition of said term in the specification (aka no human FRs).

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 113,155,156 are rejected under 35 U.S.C. § 103 as being unpatentable over Goldenberg et al. (J. Clin. Oncol.) in view of Morrison et al., Cabilly et al., Boss et al., Orlandi et al., and Huston et al. (US Patent 5,258,498). Applicants arguments have been considered and deemed not persuasive.

Goldenberg et al. teach the murine LL2 monoclonal antibody and hybridoma producing said antibody (see page 549). Goldenberg et al. teach that administration of said antibody provokes a HAMA response in some patients (see abstract). The claimed nucleic acids encode peptides which encompass or contain the CDR(s) found in the VH and VL of said antibody. The hybridoma which produces murine LL2 antibody produces the claimed nucleic acids which encode the VH and VL of said antibody. Goldenberg et al. do not teach the claimed isolated nucleic acids and vectors or host cells containing said nucleic acids. Morrison et al. teach chimeric antibodies containing variable regions from a known mouse antibody attached to human constant regions (see abstract and columns 1-8). Morrison et al. disclose nucleic acids encoding variable light and heavy chains of a murine antibody attached to nucleic acids encoding human constant regions (see column 3-6). Morrison et al. disclose that the nucleic acids encoding the murine variable regions would be obtained by routine experimentation (see column 3). The nucleic acids are expressed in vectors (see column 6, penultimate paragraph) which can be transfected into myeloma cells (see column 7, second paragraph). Orlandi et al. also teaches primers and the use of said primers to clone DNA encoding murine variable heavy and light regions (eg. see abstract and page 3833, second column and page 3834). Both Cabilly et al. and Boss et al. disclose methods for the determination of nucleic acids encoding VH and VL of any known antibody. Huston et al. teaches that regarding the determination of the sequence of VH and VL from any desired antibody that "Such sequence analysis is now conducted routinely." (see column 13).

Thus, the art taught the murine LL2 antibody, nucleic acids encoding VH and VL and methods of producing VH and VL amino acid sequences encoding any known antibody wherein said methods used a hybridoma which produced said antibody. Said nucleic acids would have been used to produce chimeric antibodies as per taught by Morrison et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Goldenberg et al. teach the murine LL2 monoclonal antibody wherein said antibody is produced by a hybridoma, and the references cited in this rejection teach chimeric antibodies, nucleic acids encoding VH and VL, and methods of making chimeric antibodies based on the nucleic acid sequence of any known antibody VH and VL, and methods of determining the nucleic acid sequence of any known antibody VH and VL. Cabilly et al. disclose that the chimeric antibodies can be produced as Fab (see column 5, first complete paragraph). All variable regions are structurally similar in that they contain similar numbers of amino acids organized in a similar fashion (eg. they contain a VH and VL wherein the VH and VL contain framework and variable region amino acids). Regarding motivation to create the claimed invention, Goldenberg et al. disclose clinical use of the murine LL2 antibody and the art recognized the advantages of antibodies encoded by nucleic acids encoding chimeric antibodies (see Morrison et al., column 7, last paragraph, continued on column 8, Orlandi et al., page 3833, first column, first paragraph).

Regarding applicants comments about the LL2 antibody, the prior art is presumed operable/enabling (aka that the LL2 was publicly available) in the absence of evidence to the contrary. The MPEP section 2121 states:

> *PRIOR ART IS PRESUMED TO BE OPERABLE/ ENABLING*
> *When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts*

rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

Regarding applicants comments, there is no evidence of record regarding the lack of public availability of the LL2 antibody or hybridoma producing said antibody. Regarding the Goldenberg and Hansen declarations, said declarations refer to vectors encoding humanized LL2 which are not germane to the instant rejection. Said declarations do not address the public availability of the LL2 antibody or hybridoma. Regarding applicants comments about the availability of the LL2 antibody, the MPEP section 716.01(c), states:
ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE The arguments of counsel cannot take the place of evidence in the record. In re *Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).*

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1600~~ 1644